AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph at page 2, line 25, though page 4, line 7, with the following amended paragraph:

Though the production of proteins can be controlled at various stages in vivo, the transcriptional regulation is the most fundamental step. Thus, modifying the level of disease-associated protein at the transcriptional stage is one of the powerful means to treat diseases. Gene transcription is regulated via the promoter and enhancer region located in neighborhood of the nucleotide sequence transcribed into messenger RNA. For transcriptional regulation, a kind of proteins, called transcriptional regulatory factors, is needed to bind to the nucleotide sequences, called the regulatory sequences, in the promoter and enhancer regions of the gene. Among those transcriptional regulatory factors, a group of proteins called nuclear receptors have a unique character that their activities can be regulated by interacting with small molecules called ligands. For example, PPARγ (peroxisome proliferator-activated receptor γ) is an important nuclear receptor for adipose differentiation. PPARγ forms a heterodimer with another nuclear receptor RXR (retinoid X receptor) and specifically binds to the regulatory sequence called PPRE (peroxisome proliferator-activated receptor responsive element) in the promoter or enhancer region of the genes. PPARγ activity is regulated by endogenous unknown ligands or exogenous ligands such as thiazolidinedione derivatives (*Annu. Rev. Biochem.*, 70:341-367, 2001). The regulatory sequence PPRE is comprised of the characteristic nucleotide sequence that is represented by 5'-AGGTCAnAGGTCA-3' (SEQ ID NO:15), which is different from every kind of genes with PPRE. When creating the medicine that can exhibit efficacy by changing the adiponectin production at the transcriptional stage, identification of the regulatory sequence in the promoter or enhancer region of the

adiponectin gene is quite useful in constructing the efficient and best screening system for

discovering potential compounds. Transformants can be created by connecting a DNA

containing the identified regulatory sequences to a suitable reporter gene, and transforming

host cells with the DNA. The transformants can be used as a useful screening system of

preventive and/or therapeutic medicines for metabolic disorder such as diabetes, obesity,

hypercholesterolemia, and hyperlipoproteinemias, *etc.*, hyperlipidemia, arteriosclerosis,

hypertonia, circulatory system disease, and hyperphagia, *etc.*, which can act through the

induction of adiponectin gene expression. Moreover, the transformants can be also used as

the useful screening system of preventive and/or therapeutic medicines for various syndromes

(Syndrome X, metabolic syndrome, multiple risk factor syndrome, insulin resistance

syndrome, deadly quartet, visceral fat syndrome, *etc.*) caused by the above diseases.

However, regulatory sequences related to the control of human adiponectin gene expression

has not been identified so far and no method can substantially and effectively screen any

accelerators of the human adiponectin gene expression.

**Please replace the paragraph at page 18, encompassing lines 15-16, with the
following amended paragraph:**

Figure 5 shows comparison of PPRE nucleotide sequences of the genes that are

transcriptionally regulated by PPARγ/RXR heterodimer, where the human adiponectin PPRE

sequence is SEQ ID NO:16, where the mouse aP2 PPRE sequences are SEQ ID NO:17

(upper) and SEQ ID NO:18 (lower), where the mouse *c*-Cbl binding protein PPRE sequence

is SEQ ID NO:19, where the mouse LXRα PPRE sequence is SEQ ID NO:20, and where the

mouse aquaporin adipose PPRE sequence is SEQ ID NO:21;

Please replace the paragraph at page 18, encompassing lines 17-18, with the

following amended paragraph:

Figure 6 shows PPRE sequence (SEQ ID NO:22) in human adiponectin gene and a

structure of human adiponectin promoter/reporter plasmid DNA mutated in PPRE sequence;